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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	
Esther H. CHANG	
Serial No. 09/716,320	Examiner: Mary M. Schmidt
Filed: November 21, 2000	Group Art Unit: 1635
For: COMPOSITIONS AND METHODS FOR REDUCING RADIATION AND DRUG RESISTANCE IN CELLS	

RESPONSE TO ELECTION REQUIREMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In an Office Action dated September 24, 2002, Applicants were advised that the above-referenced patent application contains claims directed to 35 patentably distinct species of the claimed invention and that they are required under 35 U.S.C. § 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim finally is held to be allowable. The examiner noted that currently claims 1-7, 11-16 and 20 are generic.

The 35 "species" listed in the Action are specific genes, mutations in which or the overexpression of which can lead to resistance to radiation or drug treatment, listed in claims 8 and

17 of the application. Claims 9 and 10 depend from claim 8 and each specify a particular gene; claims 18 and 19 depend from claim 17 and also each specify a particular gene.

Applicants hereby provisionally elect species 31, a gene encoding an RTK (receptor tyrosine kinase), for consideration should the generic claims ultimately not be found to be allowable. Of the generic claims, the identity of the mutated or overexpressed gene which can lead to resistance to radiation or to drug treatment, is not relevant to claims 1-2. Claims 3-7, 11-16 and 20 all encompass methods in which radiation or drug resistance of a cell could be caused by overexpression of an RTK gene. Claims 9, 10, 17 and 18 do not read on the elected species.

Applicants note that in relevant part the invention as disclosed and claimed in this application stems from the fact that cells, such as various tumor cells, can become resistant to radiation therapy or drug treatment. Studies have indicated that radiation resistant phenotype appears to be linked to the activation of specific proto-oncogenes in a signal transduction pathway. The inventors have developed a method of disrupting the pathway to effect a reversal of this drug and resistance phenotype and increase the sensitivity of resistant cells to drug/radiation therapy. The method they have developed involves

the administration of an antisense oligonucleotide to modulate the expression of specific proto-oncogenes in the signal transduction pathway which lead to the radiation resistant phenotype. More specifically, the method employs the administration of antisense oligonucleotides complementary to unique sequences of HER-2 genes such that the expression of this factor is reduced. The invention thus provides antisense oligos for reverting radiation and drug resistant cells both *in vitro* and *in vivo* for use in diagnostic assays for detecting the expression of genes in the signal transduction pathway, as listed in claims 8 and 17, which leads to radiation and/or drug resistance and for use as therapeutic agents for inhibiting tumor cell growth to improve the response to conventional therapeutic agents, thereby improving survival.

From this, and from the generic claims, it is clear that the invention has broad applicability to situations in which resistance to radiation or drug treatment is the result of the mutation or overexpression of any of a wide variety of genes. Applicants have listed a number of examples of such genes in claims 8 and 17, but this list is not comprehensive and is not intended to limit the scope of the invention in any way. This is evident by the Applicants' broad, generic claims. Applicants

respectfully request that the generic claims of this application be allowed.

Respectfully submitted,

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